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L2: Entry 1 of 4 File: USPT Aug 13, 2002

DOCUMENT-IDENTIFIER: US 6432679 B1
TITLE: Enhancement of B cell activation and immunoglobulin secretion by co-stimulation of receptors for antigen and EBV Gp350/220

Detailed Description Text (37):
In contrast, Gp350/220 sequences are highly preferred as adjuvants and adjuvanting components of immunostimulatory compositions, as compared to complement components, for the following additional reasons: 1) Antibodies raised against epitopes of the Gp350/220 adjuvant may themselves be beneficial in providing protection against EBV infection or infectivity. 2) Where the antigen linked to the complement component is of low molecular weight, the resulting construct would be of low molecular weight as well. The in vivo half-life of low molecular weight constructs is often short and this rapid elimination detracts from immunogenicity. In contrast, compositions based on the larger Gp350/220 polypeptides will be expected to have a longer effective half-life than those based on C3d. 3) Effective antigen presentation depends on cross-linking of the antigen receptors on a B cell. Because more copies of antigen can be ligated to the larger Gp350/220 proteins than to C3b, constructs based on Gp350/220 will be more antigenic. 4) Antibodies raised against CR1, CR2, or CD19 are expensive and difficult to produce. Moreover, vaccination with antibody sequences can elicit undesirable immune responses, including autoimmune reactions. 5) The safety and efficacy of Gp350/220 vaccine components has already been examined, whereas the toxicity of C3 components is uncertain. Because complement activation triggers the acute inflammatory response, it is possible that complement-based adjuvants will stimulate inflammation. 6) It has been suggested in the field that C3d-fusion proteins are difficult to synthesize and purify, possibly due to problems in folding recombinantly produced C3d polypeptides. 7) Proper folding of C3d is critical to CR2 binding. In genetically engineered constructs with antigen, there may be antigens that distort the folding of C3d and reduce or eliminate its binding to the receptor. In contrast, folding of the CR2-binding domain in the larger Gp350/220 proteins is less likely to be disrupted by fusion with antigen.

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L2: Entry 3 of 4 File: USPT Jan 29, 2002

DOCUMENT-IDENTIFIER: US 6342226 B1
TITLE: Method for increasing immunogenicity, product obtained and pharmaceutical compositions

Brief Summary Text (27):
It is possible that the observed adjuvant effect might also be mediated by an opsonisation of the particles, involving interaction between serum IgGs or complement fragments such as C3b and their respective receptors at the surface of the presenting cells.

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Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Term	Documents
C3B.DWPI,EPAB,USPT.	665
C3BS	0
CO-STIMULAT.DWPI,EPAB,USPT.	1
CO-STIMULATS	0
COSTIMULAT$	0
COSTIMULATE.DWPI,EPAB,USPT.	83
COSTIMULATED.DWPI,EPAB,USPT.	71
COSTIMULATES.DWPI,EPAB,USPT.	77
COSTIMULATIN.DWPI,EPAB,USPT.	2
COSTIMULATING.DWPI,EPAB,USPT.	72
COSTIMULATION.DWPI,EPAB,USPT.	431
((C3B) SAME (COSTIMULAT$ OR 'CO-STIMULAT$')).USPT,EPAB,DWPI.	3

There are more results than shown above. Click here to view the entire set.

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L3

Refine Search

Recall Text | Clear

Search History

DATE: Monday, November 04, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,EPAB,DWPI; PLUR=YES; OP=ADJ		
L3	(c3b) same (costimulat$ or 'co-stimulat$')	3	L3
L2	(c3b) same (adjuvant)	4	L2
L1	(c3b) same (vaccin$)	12	L1

END OF SEARCH HISTORY

2/7/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07758594 EMBASE No: 1999241376
Different stimulating effects of complement **C3b** and complete Freund's **adjuvant** on antibody response
Villiers M.-B.; Villiers C.L.; Laharie A.-M.; Marche P.N.
M.-B. Villiers, Laboratoire Immunochimie, CEA-G, DBMS-ICH, INSERM U238, Universite Joseph Fourier, 17 Rue des Martyrs, F38054 Grenoble, Cedex 9 France
AUTHOR EMAIL: immuno@dsvgre.cea.fr
Immunopharmacology (IMMUNOPHARMACOLOGY) (Netherlands) 1999, 42/1-3 (151-157)
CODEN: IMMUD ISSN: 0162-3109
PUBLISHER ITEM IDENTIFIER: S016231099900017X
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 36

Upon activation, complement C3 undergoes a conformational change and acquires the capacity to covalently bind to other proteins such as antigen and to interact with specific receptors; therefore, C3 is involved in cell mediated immune response. The adjuvant effect produced by linking CS-fragments to antigen has recently been described. We injected C3b-Ag complexes consisting of one molecule of C3b ester linked to one molecule of HEL to immunised mice, and we compared the **C3b adjuvant** activity with that of complete Freund's **adjuvant**. IgG titers elicited by HEL emulsified in CFA (HEL + CFA) were higher than those elicited by HEL-C3b, but decreased rapidly after a peak response around day 45 whereas HEL-C3b resulted in a continuous increase of anti-HEL response. Mice immunised with HEL + CFA then boosted with HEL-C3b gave significantly higher response than those boosted with HEL + CFA, indicating more efficient memory cell restimulation by C3b, HEL + CFA leads to better priming than HEL-**C3b** when mice are boosted with HEL-**C3b**. Thus, **adjuvant** effect of **C3b** is different from that of CFA, leading to more stable IgG production and better memory stimulation.

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Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Term	Documents
C3B.DWPI,EPAB.	63
C3BS	0
IMMUNIZ$	0
IMMUNIZABLE.DWPI,EPAB.	1
IMMUNIZATIO.DWPI,EPAB.	2
IMMUNIZATION.DWPI,EPAB.	1353
IMMUNIZATIONOF.DWPI,EPAB.	1
IMMUNIZATIONS.DWPI,EPAB.	94
IMMUNIZATION/VACCINATION.DWPI,EPAB.	1
IMMUNIZATION:.DWPI,EPAB.	1
IMMUNIZATONS.DWPI,EPAB.	1
((C3B) SAME (IMMUNIZ$ OR IMMUNIS$)).EPAB,DWPI.	0

There are more results than shown above. Click here to view the entire set.

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: (c3b) same (immuniz$ or immunis$)

Refine Search

Recall Text | Clear

Search History

DATE: Monday, November 04, 2002 Printable Copy Create Case

WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Term	Documents
C3B.DWPI,EPAB,USPT.	665
C3BS	0
COMPLEMENT.DWPI,EPAB,USPT.	70188
COMPLEMENTS.DWPI,EPAB,USPT.	15865
VACCIN$	0
VACCIN.DWPI,EPAB,USPT.	88
VACCINA.DWPI,EPAB,USPT.	231
VACCINAA.DWPI,EPAB,USPT.	1
VACCINAE.DWPI,EPAB,USPT.	3
VACCINAFION.DWPI,EPAB,USPT.	1
VACCINAI.DWPI,EPAB,USPT.	3
((C3B OR COMPLEMENT) SAME (VACCIN$ OR ADJUVANT$) AND C3B).USPT,EPAB,DWPI.	46

There are more results than shown above. Click here to view the entire set.

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L2

Refine Search

Recall Text | Clear

Search History

DATE: Monday, November 04, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,DWPI; PLUR=YES; OP=ADJ			
L2	(c3b or complement) same (vaccin$ or adjuvant$) and c3b	46	L2
L1	(c3b or complement) same (vaccin$ or adjuvant$)	839	L1

END OF SEARCH HISTORY

Set Name side by side	Query	Hit Count	Set Name result set
DB=EPAB,DWPI; PLUR=YES; OP=ADJ			
L7	(c3b) same (immuniz$ or immunis$)	0	L7
DB=USPT; PLUR=YES; OP=ADJ			
L6	(c3b) same (immuniz$ or immunis$)	10	L6
L5	L4 and c3b	1	L5
L4	6342226.pn.	1	L4
DB=USPT,EPAB,DWPI; PLUR=YES; OP=ADJ			
L3	(c3b) same (costimulat$ or 'co-stimulat$')	3	L3
L2	(c3b) same (adjuvant)	4	L2
L1	(c3b) same (vaccin$)	12	L1

END OF SEARCH HISTORY

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L2: Entry 10 of 46 File: USPT May 1, 2001

DOCUMENT-IDENTIFIER: US 6224870 B1
TITLE: Vaccine compositions and methods of modulating immune responses

Brief Summary Text (6):
There have been a number of attempts to increase uptake of antigens by APCs by coupling an antigen via a non-peptide linkage to another molecule that can bind to the surface of an APC. Targeting moieties have included, for example, C3b (Jacquier-Sarlin et al., Immunol 84:164-70; Arvieux et al., Immunol 65:229-35), alpha-2 macroglobulin (Chu et al, J Immunol 152:1538-45; Chu and Pizzo, J Immunol 150:48-58), and molecules comprising idiotypes specific for immunoglobulin Fc receptors (Squire et al., J Immunol 152:4388-96; Gosselin et al., J Immunol 149:3477-81; Snider and Segal, J Immunol 143:59-65) or class II MHC molecules (Estrada et al., Vaccine 13:901-7; Berg et al., Eur J Immunol 24:1262-8; Carayanniotis and Barber, Nature 327:59-61).

Brief Summary Text (16):
APC binding domains of innate opsonins encoded by the nucleic acid molecules can include, for example, an APC binding domain of fibronectin, .alpha.2macroglobulin (a2m), C-reactive protein (CRP), complement component C1q, complement fragment C3b, complement component C4b, mannose binding protein, conglutinin, and surfactant proteins A and D.

Brief Summary Text (40):
Other particularly useful opsonins bind to receptors on monocyte-lineage APCs such as receptors which play a role in innate immunity. Examples of such receptors include CR1, CR3, the C1q receptors and receptors containing a component of the C1q receptors. Examples of opsonins which can be used in the compositions and methods of the invention include fibronectin (e.g., Genbank accessions X02761, K00799, K02273, X82402, X00307, X00739), CRP (e.g., Genbank accessions X17496, M111880, M11881, M11882), complement components such as C1q (e.g., Genbank accessions X66295, M22531, X03084, X58861, and Swiss-Prot accessions P02747, P02745), complement fragments such as C3b (e.g., Genbank accessions K02782, K02765), mannose binding protein (e.g., Genbank accessions S42292, S42294, X15422), conglutinin (e.g., Genbank accession X71774), alpha-2-macroglobulin (e.g., Genbank accessions M93264, M11313), and surfactant proteins A (e.g., Genbank accessions M68519, S48768) and D (e.g., Genbank accessions L40156, X65018, S38981), and their homologues among species.

Brief Summary Text (42):
Becherer and Lambris, 1988, J Biol Chem 263:14586 describe fragments of C3b that bind to CR1, e.g., C3c, fragments of C3 generated by elastase treatment and comprising the N-terminal of the alpha' chain of C3b, and a synthetic peptide comprising the 42 N-terminal amino acids of the C3b alpha' chain. A binding sequence in C3 for CR3 has also been described (Wright et al., 1987, PNAS 84:4235).

Brief Summary Text (45):
Some sets of opsonins can be regarded as structurally and functionally similar. For example, one family comprises fragments of complement components C3 and C4. These two components are highly structurally homologous, and each possesses an intramolecular thiolester bond that is broken when a peptide (C3a or C4a respectively) is proteolytically cleaved from the native molecule. Disruption of the thiolester makes available a chemical structure that can form an ester linkage with an antigen. The moiety of C3 on which this ester bond resides, i.e. the non-C3a moiety, is designated C3b, and C4b is the analogous product of C4 cleavage. C3b can

be further proteolysed by proteins such as factor I to yield fragments such as C3bi and C3d, which also remain linked to the antigen via the ester bond.

Brief Summary Text (47):
There are four structurally unique proteins that are known to function as high affinity receptors for biologically active, membrane-bound fragments of C3 and/or C4. CR1 is the major receptor for the C3b fragment of C3 and C4b fragment of C4. It is expressed on monocytes and monocyte-derived APCs, among other cell types. CR2 is the major receptor for the fragment of C3 known as C3d, and is expressed on, e.g., mature B lymphocytes, but not on cells of monocytic lineage. The major role of CR2 on B lymphocytes is believed to be direct costimulation of B cells in concert with their cognate antigens.

Brief Summary Text (59):
A fusion polypeptide or multichain complex of the invention will bind to the antigen presenting cell via the opsonin portion of the molecule rather than via the antigen. This is easily distinguishable as free antigen will not compete with a fusion polypeptide for APC binding if the polypeptide or complex binds to the APC via the APC binding domain, whereas free antigen will compete with the fusion polypeptide binding to the APC if the polypeptide or complex binds to the APC via the antigen portion of the polypeptide or complex. Therefore, a fusion polypeptide of the invention comprises an APC binding domain of an opsonin if this APC binding domain can bind to a receptor that is physiologically expressed on an APC with an affinity at least in the nanomolar range when included in a fusion polypeptide that does not comprise a second portion, heterologous to the first opsonin, which, in isolation, can bind to a receptor that is physiologically expressed on an APC with an affinity at least in the nanomolar range. APC-binding domains that do not comprise entire opsonins have been described, for example, for mannose binding protein (Tenner et al., Immunity 3:485-95), C3b (Becherer and Lambris, J Biol Chem 263:145891), conglutinin (Malhotra et al., Biochem J 293:15-19), and fibronectin (Czop and Austen, J Immunol 129:2678-81).

Brief Summary Text (108):
The term "antigen" as used herein refers to a molecule which can initiate a humoral and/or cellular immune response in a recipient of the antigen. The antigen is preferably an agent that causes a disease for which a vaccination would be advantageous treatment. The antigen portion of the fusion polypeptide is preferably at least 8 amino acids, and is preferably no longer than 25 amino acids, and preferably does not include more than 10 contiguous amino acids of an opsonin, or a lectin binding domain of a eukaryotic intercellular adhesion molecule, or a reporter molecule such as .beta.-galactosidase. As used herein, a "lectin binding domain" refers to a carboxy-terminal carbohydrate recognition domain of a protein, for example exon 4, nucleotides 439-813 of human mannose binding protein. "Complement-fixing domain" refers to a collagen-like segment having a repeated pattern of Gly-X-Y (where X and Y represent any amino acid) similar to those of non-fibriallar collagen genes. The structure is consistent with those of an effector region which interacts with complement components; for example, exon 2, nucleotides 253-369 of human mannose binding protein.

Detailed Description Text (3):
A fusion gene incorporating sequences for the pneumococcal antigen pneumolysin and for the alpha chain of the opsonin murine C3b is generated using the following method.

Detailed Description Text (4):
The sequence encoding the alpha chain of murine C3b is amplified by PCR from mouse liver cDNA using an upstream primer corresponding to nt 2301-2324 of Genbank K02782, and a downstream primer complementary to nt 5018-5045. The gene for pneumolysin is amplified from pneumococcal DNA using an upstream primer corresponding to nucleotides 207-233 of Genbank M17717 and flanked on the 5' end by 12 bases that correspond to nt 5034-5045 of Genbank K02782 and a downstream primer that corresponds to the sequence complementary to nucleotides 599-1622 of M17717 and flanked at the 5' end by a Sph I site. Both products are isolated by agarose gel electrophoresis, eluted using glass beads, and used, in equimolar amounts, in a PCR reaction with excess amounts of the upstream C3b alpha chain primer and the

downstream pneumolysin primer. The fusion product is isolated by agarose gel electrophoresis and digested with Sph I. A double-stranded DNA sequence corresponding to the mouse IL-2 secretory sequence (nt 48-107 of Genbank X01772) and flanked upstream by a single-stranded Hind III overhang is prepared. The mammalian expression vector pcDNA3 is digested with Hind III and Sph I, and the fragments are ligated into the plasmid so that the CMV promoter is upstream of the IL-2 signal sequence, which is upstream of the C3b alpha chain/pneumolysin fusion gene.

Detailed Description Text (23):
In this example, three units of the same opsonin are included in one polypeptide. The sequence encoding the alphaAE chain of murine C3b is amplified in three ways: in one reaction, the downstream primer includes a sequence that can be annealed in-frame to the upstream end of the sequence obtained in a second reaction. The downstream end of the second sequence is designed to anneal in-frame to the upstream end of a sequence obtained in a third reaction. The downstream end of the third C3b alphaAE encoding sequence is designed to anneal in-frame to a sequence encoding a polypeptide chain of telomerase, a tumor antigen. The construct can be cloned into a secretory expression vector which places the murine IL-2 secretory sequence in-frame upstream of the first C3 b.

Other Reference Publication (10):
Arvieux et al., 1988, Antigen-bound C3b and B4b enhance antigen-presenting cell function in activation of human T-cell clones, Immunology 65: 229-235.

Other Reference Publication (12):
Becherer and Lambris, 1988, Identification of the C3b receptor-binding comain in third component of complement, J. Biol. Chem. 263: 14586-14591.

Other Reference Publication (19):
Dempsey et al., 1996, C3d of complement as a molecular adjuvant: bridging innate and acquired immunity, Science 271: 348-350.

Other Reference Publication (28):
Jacquier-Sarlin et al., 1995, Modulation of antigen processing and presentation by covalently linked complement C3b fragment, Immunology 84: 164-170.

Other Reference Publication (30):
Lambris and Ross, 1982, Assay of membrane complement receptors (CR.sub.1 and CR.sub.2) with C3b- and C3d-coated fluorescent microspheres, J. Immunol. 128: 186-189.

CLAIMS:

3. The method of claim 2 wherein said APC binding domain of said opsonin is a domain of an opsonin selected from the group of opsonins consisting of: Fibronectin, C3, a collectin, alpha-2 macroglobulin, C-reactive protein, complement component C1q, complement fragment C3b, complement component C4b, mannose binding protein, conglutinin, surfactant protein A, and surfactant protein D.

7/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09111209 BIOSIS NO.: 199497119579
A glycosylphosphatidylinositol-anchored cytokine can function as an artificial cellular adhesin.
AUTHOR: Weber Matthew C; Groger Richard K; Tykrocinski Mark L(a)
AUTHOR ADDRESS: (a)Inst. Pathol., Case Western Reserve Univ., Cleveland, OH 44106**USA
JOURNAL: Experimental Cell Research 210 (1):p107-112 **1994**
ISSN: 0014-4827
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A novel strategy for altering the adhesive properties of cells has been developed which is based upon the use of artificial adhesins. Specifically, a **glycosylphosphatidylinositol** (**GPI**)-modified variant of the **cytokine** macrophage colony stimulating factor (M-CSF), designated M-CSF cntdot **GPI**, was expressed on the surface of human bone marrow stromal cells. A chimeric M-CSF:decayaccelerating factor expression construct was used for M-CSF cntdot **GPI** expression. Cell:cell binding assays established that this artificially membrane-tethered **cytokine** functions as a potent cellular adhesin, allowing for enhanced binding to M-CSF receptor-expressing cellular transfectants. **Antibody** blocking analyses confirmed the M-CSF:M-CSF receptor dependence of the enhanced intercellular binding. This capacity to direct the cellular interactive repertoire of selected cells can in principle be applied to other cell types and other molecular pairs to be used in cell-based therapies.

7/7/25 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08197629 94331621 PMID: 8054537

Regulation of T lymphocyte function by glycosylphosphatidylinositol (GPI)-anchored proteins.

Malek T R; Fleming T J; Codias E K

Department of Microbiology and Immunology, University of Miami School of Medicine, FL 33101.

Seminars in immunology (UNITED STATES) Apr **1994**, 6 (2) p105-13
, ISSN 1044-5323 Journal Code: 9009458

Contract/Grant No.: R01 CA46096; CA; NCI; T32 AI107346; AI; NIAID

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Monoclonal **antibody** binding to **GPI**-anchored proteins, e.g. Thy-1 and Ly-6, on the surface of T lymphocytes usually leads to stimulation of **interleukin**-2 production. This phenomenon is dependent upon expression of the zeta-chain of the T cell receptor complex and requires the **GPI** anchor. Recent studies suggest that this activation may proceed through a common pathway resulting in tyrosine phosphorylation of intracellular substrates and association of various GPI-anchored proteins to src-family tyrosine kinases. Several models are discussed to explain the signaling capabilities of GPI-anchored proteins. In contrast, under some experimental conditions antibody binding to selected GPI-anchored proteins, i.e. Ly-6A/E and sgp60 (CD48), leads to inhibition of T cell activation. Furthermore, induction of Ly-6A/E expression on CD4 effector T cells correlates with a decreased capacity to secrete IL-2. These latter results suggest that Ly-6A/E may also function to down-regulate an immune response. (59 Refs.)

Record Date Created: 19940909

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File 410:Chronolog(R)  1981-2002/Sep
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     $0.04  TELNET
     $0.04  Estimated cost this search
     $0.40  Estimated total session cost   0.173 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2002/Oct W4
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*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  73:EMBASE  1974-2002/Oct W4
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*File  73: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File 155:MEDLINE(R)  1966-2002/Oct W4
*File 155: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File 399:CA SEARCH(R)  1967-2002/UD=13718
         (c) 2002 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
Alert feature enhanced for multiple files, etc. See HELP ALERT.

      Set  Items  Description
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? s (vaccin?) and lipid and (gpi or glycosylphosphatidylinositol)
          362083  VACCIN?
          663942  LIPID
           12642  GPI
            7325  GLYCOSYLPHOSPHATIDYLINOSITOL
      S1      28  (VACCIN?) AND LIPID AND (GPI OR
                  GLYCOSYLPHOSPHATIDYLINOSITOL)
? rd s1
...completed examining records
      S2      12  RD S1 (unique items)
? t s12/7/all
>>>Set 12 does not exist
? t s2/7/all

 2/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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13024188   BIOSIS NO.: 200100231337
GPI-anchored proteins: Now you see 'em, now you don't.
AUTHOR: Butikofer Peter; Malherbe Tatiana; Boschung Monika; Roditi Isabel
  (a)
AUTHOR ADDRESS: (a)Institute of Cell Biology, University of Bern,
  Baltzerstrasse 4, 3012, Bern: isabel.roditi@izb.unibe.ch**Switzerland
JOURNAL: FASEB Journal  15 (2):p545-548 February, 2001
MEDIUM: print
ISSN: 0892-6638
DOCUMENT TYPE: Article
```

RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Many cell surface proteins are attached to membranes via covalent **glycosylphosphatidylinositol** (**GPI**) anchors that are posttranslationally linked to the carboxy-terminus of the protein. Removal of the **GPI lipid** moieties by enzymes such as **GPI**-specific phospholipases or by chemical treatments generates a soluble form of the protein that no longer associates with **lipid** bilayers. We have found that the removal of **lipid** moieties from the anchor can also have a second, unexpected effect on the antigenicity of a variety of **GPI**-anchored surface molecules, suggesting that they undergo major conformational changes. Several antibodies raised against **GPI**-anchored proteins from protozoa and mammalian cells were no longer capable of binding the corresponding antigens once the **lipid** moieties had been removed. Conversely, antibodies raised against soluble (delipidated) forms reacted poorly with intact **GPI**-anchored proteins, but showed enhanced binding after treatment with phospholipases. In the light of these findings, we have reevaluated a number of publications on **GPI**-anchored proteins. Many of the results are best explained by **lipid**-dependent changes in antigenicity, indicating this might be a widespread phenomenon. Since many pathogen surface proteins are **GPI**-anchored, researchers should be aware that the presence or absence of the **GPI lipid** moieties may have a major impact on the host immune response to infection or **vaccination**.

2/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12920048 BIOSIS NO.: 200100127197
Mutant RBL mast cells defective in FcepsilonRI signaling and **lipid** raft biosynthesis are reconstituted by activated Rho-family GTPases.
AUTHOR: Field Kenneth A; Apgar John R; Hong-Geller Elizabeth; Siraganian Reuben P; Baird Barbara; Holowka David(a)
AUTHOR ADDRESS: (a)Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY: dah24@cornell.edu**USA
JOURNAL: Molecular Biology of the Cell 11 (10):p3661-3673 October, 2000
MEDIUM: print
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Characterization of defects in a variant subline of RBL mast cells has revealed a biochemical event proximal to IgE receptor (FcepsilonRI)-stimulated tyrosine phosphorylation that is required for multiple functional responses. This cell line, designated B6A4C1, is deficient in both FcepsilonRI-mediated degranulation and biosynthesis of several **lipid** raft components. Agents that bypass receptor-mediated Ca2+ influx stimulate strong degranulation responses in these variant cells. Cross-linking of IgE-FcepsilonRI on these cells stimulates robust tyrosine phosphorylation but fails to mobilize a sustained Ca2+ response. FcepsilonRI-mediated inositol phosphate production is not detectable in these cells, and failure of adenosine receptors to mobilize Ca2+ suggests a general deficiency in stimulated phospholipase C activity. Antigen stimulation of phospholipases A2 and D is also defective. Infection of B6A4C1 cells with **vaccinia** virus constructs expressing constitutively active Rho family members Cdc42 and Rac restores antigen-stimulated degranulation, and active Cdc42 (but not active Rac)

restores ganglioside and **GPI** expression. The results support the hypothesis that activation of Cdc42 and/or Rac is critical for FcepsilonRI-mediated signaling that leads to Ca2+ mobilization and degranulation. Furthermore, they suggest that Cdc42 plays an important role in the biosynthesis and expression of certain components of **lipid** rafts.

2/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12801397 BIOSIS NO.: 200100008546
Effect of immunological adjuvant combinations on the antibody and T-cell response to **vaccination** with MUC1-KLH and GD3-KLH conjugates.
AUTHOR: Kim Soo Kie; Ragupathi Govindaswami; Cappello Sarah; Kagan Ella; Livingston Philip O(a)
AUTHOR ADDRESS: (a)Laboratory of Developmental Tumor Vaccinology, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, 10021**USA
JOURNAL: Vaccine 19 (4-5):p530-537 15 October, 2000
MEDIUM: print
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: A year ago we described a comparison of 19 immunological adjuvants for their ability to augment antibody and T-cell responses against **vaccines** containing two cancer antigens, GD3 ganglioside and MUC1 peptide, covalently attached to keyhole limpet hemocyanin (KLH). As in our previous experience, the saponin fraction QS-21 was the most potent single adjuvant but several other adjuvants also had potent adjuvant activity. Induction of an immune response against cancer antigens is generally difficult because these antigens are autoantigens. To get maximal benefit from the adjuvant component of cancer **vaccines** we have now tested whether combinations of the optimal adjuvants induced an improved immune response compared to QS-21 alone. Since over the intervening year a new semi-synthetic saponin adjuvant (**GPI**-0100) containing the dodecylamide derivative of hydrolyzed naturally-occurring saponins had become available, this was tested as well. Twelve different adjuvant combinations and **GPI**-0100 were compared for their ability to augment (1) antibody responses against GD3 and MUC1 and (2) T-cell responses against GD3, MUC1 and KLH. **GPI** -0100 and five adjuvant combinations were superior to QS-21 alone for induction of IgM and IgG antibodies against MUC1 and/or GD3: QS-21 plus bacterial nucleotide CpG, QS-21 plus monophosphoryl **lipid** A (MPL), QS-21 plus non-ionic block copolymer CRL-1005, QS-21 plus Titermax and Titermax plus CpG. Antibody responses were documented both by ELISA against purified antigens and by FACS for cell surface reactivity. There was no evidence for T-cell immunity against GD3 or MUC1. The antibody responses against GD3 and MUC1 were, however, strongly correlated with IFN-gamma release and DTH against KLH. These results demonstrate that combinations of immunological adjuvants are able to augment antibody and T-cell responses to these conjugates beyond that attainable with QS-21 alone, and again confirm the absolute necessity of potent adjuvants or adjuvant combinations for optimal immunogenicity with conjugate **vaccines**.

2/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12526219 BIOSIS NO.: 200000279721
Oligomerization, secretion, and biological function of an anchor-free parainfluenza virus type 2 (PI2) fusion protein.
AUTHOR: Tong Suxiang; Compans Richard W
AUTHOR ADDRESS: (a)Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, GA, 30322**USA
JOURNAL: Virology 270 (2):p368-376 May 10, 2000
MEDIUM: print.
ISSN: 0042-6822
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: A number of studies indicate that the transmembrane domain, the cytoplasmic domain, or both regions of viral surface glycoproteins are involved in quaternary structure formation. In this report, the transmembrane domain and cytoplasmic tail coding sequence of the fusion (F) glycoprotein gene from parainfluenza type 2 virus was truncated by PCR and the resulting gene (PI2F') was expressed in HeLa-T4 cells by using the **vaccinia** virus-T7 transient expression system. Pulse-chase experiments indicated that the anchor-free PI2F' was expressed and processed into F1 and F2 subunits. Both the processed and the unprocessed anchor-free PI2F' proteins were found to be efficiently secreted into the culture medium. Examination of the oligomeric form of the anchor-free PI2F' by chemical cross-linking demonstrated that it assembles posttranslationally into dimers and trimers with a pattern similar to that of the wild-type PI2F protein. In an effort to better understand the biological properties of the truncated form of PI2F', we anchored PI2F' by a glycosyl-phosphatidylinositol (**GPI**) linkage. The **GPI**-anchored PI2F' protein, when coexpressed with PI2HN, did not induce cell fusion seen as syncytium formation, but was found to initiate **lipid** mixing (hemifusion) as observed by transfer of R-18 rhodamine from red blood cells to the **GPI**-PI2F'/PI2HN cotransfected cells. The results therefore indicate that the extracellular domain of the PI2 fusion protein contains not only the structural information sufficient to direct assembly into higher oligomers, but also is competent to initiate membrane fusion, suggesting that the anchor-free PI2F' may be useful for further structural studies.

2/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11948271 BIOSIS NO.: 199900194380
Plasmodium vivax, P. cynomolgi, and P. knowlesi: Identification of homologue proteins associated with the surface of merozoites.
AUTHOR: Barnwell John W(a); Galinski Mary R; DeSimone S Giovanni; Perler Francine; Ingravallo Paul
AUTHOR ADDRESS: (a)Department of Medical and Molecular Parasitology, New York University School of Medicine, 341 Ea**USA
JOURNAL: Experimental Parasitology 91 (3):p238-249 March, 1999
ISSN: 0014-4894
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have identified a Plasmodium vivax merozoite surface protein (MSP) that migrates on SDS-polyacrylamide gels at a Mr of about 185 kDa. This protein was recognized by a P. vivax monoclonal antibody (mAb) that localizes the protein by immunofluorescence to the surface of merozoites and also immunoprecipitates this protein from NP-40 detergent extracts of (35S)methionine metabolically radiolabeled P. vivax schizonts. The P.

vivax MSP does not become biosynthetically radiolabeled with (3H)glucoamine, (3H)myristate, (3H)palmitate, or (3H)mannose, indicating that this P. vivax MSP is not posttranslationally modified and bound to the merozoite membrane by a **glycosylphosphatidylinositol** (**GPI**) **lipid** anchor. Thus, in this respect, this protein is different from members of the MSP-1 protein family and from MSP-2 and MSP-4 of P. falciparum. The mAb cross-reacts with and outlines the surface of P. cynomolgi merozoites and immunoprecipitates a 150-kDa P. cynomolgi homologue. The mAb was used as an affinity reagent to purify the native homologous MSP from NP-40 extracts of P. cynomolgi mature schizonts in order to develop a specific polyclonal antiserum. The resulting anti-PcyMSP rabbit antiserum cross-reacts strongly with the P. vivax 185-kDa MSP and also recognizes an analogous 110-kDa protein from P. knowlesi. We have determined via an immunodepletion experiment that the 110-kDa P. knowlesi MSP corresponds to the PK 110 protein partially characterized earlier (Perler et al. 1987). The potential of P. vivax MSP as a **vaccine** candidate was addressed by conducting in vitro inhibition of erythrocyte invasion assays, and the IgG fraction of both the P. vivax MSP mAb and the P. cynomolgi MSP rabbit antiserum significantly inhibited entry of P. vivax merozoites. We denote, on a preliminary basis, these antigenically related merozite surface proteins PvMSP-185, PcyMSP-150, and PkMSP-110.

2/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10143707 BIOSIS NO.: 199698598625
Boosting immune response with a candidate varicella-zoster virus glycoprotein subunit **vaccine**.
AUTHOR: Vafai Abbas
AUTHOR ADDRESS: Dep. Biomed. Sci., Univ. Illinois, Coll. Med., Rockford, IL 61107-1897**USA
JOURNAL: Vaccine 13 (14):p1336-1338 1995
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A varicella-zoster virus (VZV) seropositive individual was immunized with 100 mu-g of purified VZV TgpI-511 glycoprotein subunit antigen formulated with monophosphoryl **lipid** A. Serum samples were obtained during a 40-day period post-immunization (PI) and analysed by immunoprecipitation and virus neutralization tests. The results from immunoprecipitation studies revealed an increase in VZV anti-**gpI** antibody titer as early as 6 days PI which continued to rise during 40 days PI. In addition, virus neutralization tests showed a 21.0% VZV neutralization 6 days PI with an increase to a 96.7% VZV neutralization 40 days PI. These results suggested that the candidate VZV glycoprotein subunit **vaccine** (TgpI-511) was capable of boosting the production of neutralizing antibodies in the immunized VZV seropositive human subject.

2/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10015570 BIOSIS NO.: 199598470488
Construction, purification, and functional incorporation on tumor cells of glycolipid-anchored human B7-1 (CD80).
AUTHOR: McHugh Rebecca S; Ahmed S Nawaz; Wang Yi-Chong; Sell Kenneth W; Selvaraj Periasamy(a)

AUTHOR ADDRESS: (a)Dep. Pathol. Lab. Med., Emory Univ., Atlanta, GA 30322** USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 92 (17):p8059-8063 1995
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: To generate a potent cell-mediated immune response, at least two signals are required by T cells. One is engagement of the T-cell receptor with peptide-bearing major histocompatibility complex molecules. The other signal can be delivered by various molecules on the antigen-presenting cell, such as B7-1 (CD80). Many tumor cells escape immune recognition by failing to express these costimulatory molecules. Transfection of the B7 gene into some murine tumor cells allows for immune recognition and subsequent rejection of the parental tumor. We have studied an alternative approach for the introduction of B7-1 onto the surface of tumor cells. This method involves purified glycosyl-phosphatidylinositol (**GPI**)-anchored proteins which can spontaneously incorporate their **lipid** tail into cell membranes. We have created and purified a **GPI**-anchored B7-1 molecule (called **GPI**-B7) which is able to bind its cognate ligand, CD28, and incorporate itself into tumor cell membranes after a short incubation. Tumor cells that have been reconstituted with **GPI**-B7 can provide the costimulatory signal needed to stimulate T cells. These findings suggest an approach for the introduction of new proteins onto cell membranes to create an effective tumor **vaccine** for potential use in human immunotherapy.

2/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06116379 BIOSIS NO.: 000085079529
LIPOPHOSPHOGLYCAN OF LEISHMANIA MAJOR THAT **VACCINATES** AGAINST CUTANEOUS LEISHMANIASIS CONTAINS AN ALKYLGLYCEROPHOSPHOINOSITOL **LIPID** ANCHOR
AUTHOR: MCCONVILLE M J; BACIC A; MITCHELL G F; HANDMAN E
AUTHOR ADDRESS: WALTER ELIZA HALL INST. MED. RES., MELBOURNE, VICTORIA 3050, AUST.
JOURNAL: PROC NATL ACAD SCI U S A 84 (24). 1987. 8941-8945. 1987
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The major cell surface glycoconjugate of Leishmania major, a putative parasite receptor for macrophages, is a lipophosphoglycan containing 81.6% (wt/wt) carbohydrate, 17.0% (wt/wt) phosphate, and 1.4% (wt/wt) **lipid**. It has been purified to homogeneity by hydrophobic chromatography and consists of a polydisperse family of molecules with Mr 5000-40,000. It contains galactose, mannose, glucose, arabinose, glucosamine, and inositol in the molar ratio of 51:21:5:6:1:1. The lipophosphoglycan has a complex structure, consisting mainly of tri- and tetrasaccharide units linked by phosphodiester bonds, which are cleaved by HF hydrolysis. The phosphate groups are located on the 6-hydroxyl of both galactose and mannose residues. The lipophosphoglycan is anchored to the parasite surface by a 1-O-alkyl-sn-glycero-3-phosphoinositol moiety. This conclusion is supported by analysis of the products of nitrous acid deamination, HF hydrolysis, and Staphylococcus aureus phosphatidylinositol specific-phospholipase C treatment. The 24:0 and

26:0 alkyl chains accounted for 93% of the ether-linked fatty acids in the **lipid** anchor. The results are also consistent with a glycosidic linkage between the inositol and a non-N-acetylated glucosamine residue. The lipophosphoglycan membrane anchor shares limited structural homology with the **glycosylphosphatidylinositol** anchors of several eukaryotic proteins, indicating that this type of membrane anchor is not limited to proteins. **Vaccination** of mice with the purified L. major lipophosphoglycan in liposomes induced resistance against cutaneous leishmaniasis.

2/7/9 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11362255 EMBASE No: 2001375898
Human immunodeficiency virus and host cell lipids. Interesting pathways in research for a new HIV therapy
Raulin J.
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Progress in Lipid Research (PROG. LIPID RES.) (United Kingdom) 2002, 41/1 (27-65)
CODEN: PLIRD ISSN: 0163-7827
PUBLISHER ITEM IDENTIFIER: S0163782701000194
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 217

It has been reported in the literature that biological membranes arising from HIV-induced cell fusion, as well as syncytium formation between infected and non-infected cells and those involved in transduction, viral DNA nuclear import and virion budding from the host cell, are all made of proteins, a phospholipid (P) bilayer and cholesterol (C). However, the P/C molar ratio is higher in the retroviral envelope than in the plasma membrane where they originate, and higher than in the nuclear envelope. Mechanisms are described which elucidate this puzzling fact, as well as cholesterol-dependent leakage and pore formation during cell fusion. Fatty acylation of viral and host cell proteins is required to direct them to membranes. Detergent-insoluble microdomains enriched in cholesterol and sphingolipids, termed either DIGs (detergent-insoluble glycolipid-enriched complexes), DRMs (detergent resistant membranes), TIFFs (Triton-insoluble floating fractions) or GEMs (glycolipid-enriched membranes), function as platforms for attachment of proteins in the process of signal transduction. HIV-SUgp120 (HIV-surface glycoprotein), T-cell receptor (TCR)-CD4+ and co-receptors promote aggregation of these **lipid** 'rafts' which concentrate the Src family tyrosine kinases SFKs (PTK, Lyn, Fyn, Lck), **GPI** (glycosyl phosphatidylinositol)-anchored proteins, and phosphatidylinositol kinases PI(3)K and PI(4)K, inducing cell signalling. HIV-SUgp120 transduces the activation signal and provokes the formation of polyunsaturated fatty acid (PUFA) metabolites, i.e. the prostaglandin PGE2 suppressor of immune function and inhibitor of cytotoxic T-lymphocyte (CTL) proliferation, while PGB2 activates SFKs and increases mRNA expression, as well as NFkappaB (nuclear transcription factor) translocation to nucleus. HIV nuclear import, DNA integration, chromatin template capacity may be mediated by the **lipid** environment. The **lipid**-enriched microdomains from which HIV-1 buds, may explain the high level of cholesterol and sphingolipids in the viral envelope, since host cell rafts become a viral coat. HIV-1 infection induces alteration of cellular lipids: (1) shift in phospholipid synthesis to neutral lipids associated with the viral load, polyunsaturated fatty acid (PUFA) peroxidation, and n-3 deficiency with deregulation of cytokines and PPAR-gamma (peroxisome proliferator-activated receptor-gamma), and (2) alloimmune phospholipid

antibody production in which antibodies to cardiolipin and to phosphatidylserine are most prevalent, due to the destruction of mitochondrial membranes and progression of lymphocyte apoptosis. The current highly active anti-retroviral therapy, including both viral reverse transcriptase (RT) inhibitors (NRTIs and NNRTIs, nucleoside and non-nucleoside RT inhibitors) and protease inhibitors (PIs), induces side-effects in the long term. Lipodystrophy (LD), consists of peripheral lipoatrophy associated with central fat accumulation (called 'crixbelly' and 'buffalo hump'), insulin resistance, elevation of very low density lipoproteins, decrease in high density lipoproteins and inhibition of adipocyte differentiation. LD syndrome appears to be induced by PIs that inhibit GLUT4, glucose transporter isoform, and by NRTIs which provoke mitochondrial failure. New therapeutic strategies assessed: (1) inhibition of the viral integrase and/or HIV entry into cells through natural products or their derivatives, (2) inhibition of HIV-1 entry into macrophages pretreated with Gram-negative bacterial lipopolysaccharide, (3) **vaccination** with multi-lipopeptides, i.e. sequences of HIV-1 peptides with CD4+ T-cell and B-cell epitopes, modified by adding a **lipid** tail to one end, which produce HIV-specific CTL and multispecific immune responses in most of the **vaccinated** subjects and (4) stimulation of antiviral drug activity with **lipid**-prodrugs targeting viral RT, polymerase, integrase, or aspartyl-protease. Copyright (c) 2001 Elsevier Science Ltd.

2/7/10 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11042897 EMBASE No: 2000355122
Effect of immunological adjuvant combinations on the antibody and T-cell response to **vaccination** with MUC1-KLH and GD3-KLH conjugates
Soo Kie Kim; Ragupathi G.; Cappello S.; Kagan E.; Livingston P.O.
P.O. Livingston, Lab. of Devmtl. Tumor Vaccinology, Memorial Sloan-Kettering Cancer Ctr., Box 113, 1275 York Avenue, New York, NY 10021 United States
Vaccine (VACCINE) (United Kingdom) 15 OCT 2000, 19/4-5 (530-537)
CODEN: VACCD ISSN: 0264-410X
PUBLISHER ITEM IDENTIFIER: S0264410X0000195X
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 23

A year ago we described a comparison of 19 immunological adjuvants for their ability to augment antibody and T-cell responses against **vaccines** containing two cancer antigens, GD3 ganglioside and MUC1 peptide, covalently attached to keyhole limpet hemocyanin (KLH). As in our previous experience, the saponin fraction QS-21 was the most potent single adjuvant but several other adjuvants also had potent adjuvant activity. Induction of an immune response against cancer antigens is generally difficult because these antigens are autoantigens. To get maximal benefit from the adjuvant component of cancer **vaccines** we have now tested whether combinations of the optimal adjuvants induced an improved immune response compared to QS-21 alone. Since over the intervening year a new semi-synthetic saponin adjuvant (**GPI**-0100) containing the dodecylamide derivative of hydrolyzed naturally-occurring saponins had become available, this was tested as well. Twelve different adjuvant combinations and **GPI**-0100 were compared for their ability to augment (1) antibody responses against GD3 and MUC1 and (2) T-cell responses against GD3, MUC1 and KLH. **GPI**-0100 and five adjuvant combinations were superior to QS-21 alone for induction of IgM and IgG antibodies against MUC1 and/or GD3: QS-21 plus bacterial nucleotide CpG, QS-21 plus monophosphoryl **lipid** A (MPL), QS-21 plus non-ionic block copolymer CRL-1005, QS-21 plus Titermax and Titermax plus CpG. Antibody responses

were documented both by ELISA against purified antigens and by FACS for cell surface reactivity. There was no evidence for T-cell immunity against GD3 or MUC1. The antibody responses against GD3 and MUC1 were, however, strongly correlated with IFN-gamma release and DTH against KLH. These results demonstrate that combinations of immunological adjuvants are able to augment antibody and T-cell responses to these conjugates beyond that attainable with QS-21 alone, and again confirm the absolute necessity of potent adjuvants or adjuvant combinations for optimal immunogenicity with conjugate **vaccines**. (C) 2000 Elsevier Science Ltd.

2/7/11 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

05408298 EMBASE No: 1993176397
Molecular variation in Leishmania
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Acta Tropica (ACTA TROP.) (Netherlands) 1993, 53/3-4 (185-204)
CODEN: ACTRA ISSN: 0001-706X
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The surface coat of the protozoan parasite Leishmania affords remarkable protection in the harsh environments encountered within the insect vectors and vertebrate hosts. It also provides specificity for the interaction of these parasites with the cells in the sandfly gut and with the human macrophage. Surprisingly few molecules have been identified on the Leishmania surface. The major surface molecules of both promastigotes and amastigotes are the glycoconjugates lipophosphoglycan and a glycoprotein of approximately 63 kDa. These major surface molecules vary structurally between Leishmania species and throughout the life-cycle of the parasite. In addition to these major glycoconjugates, Leishmania produce a number of less abundant surface molecules, including a family of glycosylinositol phospholipids, the Promastigote Surface Antigen-2 complex of glycoproteins and a glycoprotein of M(r) 46000. These molecules share the common feature of attachment to the plasma membrane via **glycosylphosphatidylinositol lipid** anchors. Leishmania also release molecules from their surface in a species specific manner. In this review we will examine the molecular variation of these molecules and their biological importance. We will also discuss the potential of these molecules as targets for chemotherapy and as candidate **vaccines**.

2/7/12 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

133221581 CA: 133(16)221581g PATENT
Modified polypeptides for enhanced immunogenicity
INVENTOR(AUTHOR): Fasel, Nicolas Joseph; Reymond, Christophe Dominique
LOCATION: Switz.
ASSIGNEE: Rmf Dictagene S.A.
PATENT: United States ; US 6113917 A DATE: 20000905
APPLICATION: US 428616 (19950425)
PAGES: 9 pp. CODEN: USXXAM LANGUAGE: English CLASS: 424268100; A61K-039/00A; A61K-039/002B; A61K-039/015B; C12P-021/06B
SECTION:
CA215002 Immunochemistry
IDENTIFIERS: polypeptide GPI anchor immunogenicity
DESCRIPTORS:
Vaccines...
antimalarial; enhanced immunogenicity of GPI-anchored circumsporozoite

protein in relation to
Proteins,specific or class...
contact site A, fusion products with circumsporozoite protein; enhanced immunogenicity of
Antigens...
CS (circumsporozoite), fusion products, with GPI anchor; enhanced immunogenicity of
Parasite...
enhanced immunogenicity of GPI-anchored antigens of
Plasmodium falciparum...
enhanced immunogenicity of GPI-anchored circumsporozoite protein of
Dictyostelium discoideum...
expression of GPI-anchored antigens in
Protein motifs...
glycolipid anchor addn. sequence; of chimeric proteins in relation to enhanced immunogenicity
Antigens...
GPI-anchored; enhanced immunogenicity of
Glycophospholipids...
phosphatidylinositol-contg.; enhanced immunogenicity of polypeptides engineered with site for
Antibodies...
to GPI-anchored circumsporozoite protein of Plasmodium falciparum
Antimalarials...
vaccines; enhanced immunogenicity of GPI-anchored circumsporozoite protein in relation to
CAS REGISTRY NUMBERS:
290873-74-4 290873-75-5 290873-76-6 290873-77-7 290873-78-8
290873-79-9 290873-80-2 unclaimed nucleotide sequence; modified polypeptides for enhanced immunogenicity
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